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10/572,348	12/18/2006	Jesper Lau	6692.204-US	7549

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/572,348	LAU ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75-146* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *75-146* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 76-123, 126-128, 138, and 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is GLP-1, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 2, claim(s) 76-111, 124, 128, 138 and 140-141, drawn to drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is exendin-4, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 3, claim(s) 76-111, 125, 128, 138 and 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is ZP-10 (i.e., HGEGTFTSDLSKQMEEEAVRLFIEWLKNGGPSSGAPPSKKKKKK-amide), hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 4, claims 76-110, 129-132, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is GLP-2, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 5, claims 76-110, 133-134, 138,140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is human insulin, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 6, claims 76-110, 135, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer,

wherein therapeutic polypeptide is human growth hormone or an analog thereof, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 7, claims 76-110, 136, 138, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is parathyroid hormone or an analog thereof, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 8, claims 76-110, 137, 138, 140-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is follicle stimulating hormone or an analog thereof, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 9, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a growth factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 10, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a somatomedin, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 11, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a interferon, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 12, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a pro-urokinase or urokinase, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 13, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a tissue plasminogen activator (t-PA), hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 14, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a plasminogen activator inhibitor 1, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 15, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a plasminogen activator inhibitor 2, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 16, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a von Willebrandt factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 17, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a cytokine, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 18, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a colony stimulating factor (CFS), hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 19, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a stem cell factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 20, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a tumor necrosis factor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 21, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a protease inhibitor, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 22, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is an opioid, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 23, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a hormone, hydrophilic spacer is $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 24, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a neuropeptide, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 25, claims 76-110, 138, 139-141, drawn to a compound which comprises a therapeutic polypeptide linked to an albumin binding residue via a hydrophilic spacer, wherein therapeutic polypeptide is a melanocortin, hydrophilic spacer is -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 26, claims 142-143, drawn to a method of treating type 2 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 27, claim 142, drawn to a method of treating hyperglycemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 28, claim 142, drawn to a method of treating impaired glucose tolerance in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 29, claim 142, drawn to a method of treating type 1 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 30, claim 142, drawn to a method of treating obesity in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 31, claim 142, drawn to a method of treating hypertension in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 32, claim 142, drawn to a method of treating syndrome X in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 33, claim 142, drawn to a method of treating dyslipidemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 34, claim 142, drawn to a method of treating cognitive disorders in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 35, claim 142, drawn to a method of treating atheroschlerosis in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 36, claim 142, drawn to a method of treating myocardial infarction in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 37, claim 142, drawn to a method of treating coronary heart disease in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 38, claim 142, drawn to a method of treating stroke in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 39, claim 142, drawn to a method of treating inflammatory bowel syndrome in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 40, claim 142, drawn to a method of treating dyspepsia or gastric ulcer in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 41, claim 144, drawn to a method of decreasing food intake in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 42, claim 144, drawn to a method of decreasing β-cell apoptosis in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 43, claim 144, drawn to a method of increasing β-cell function and β-cell mass in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 44, claim 144, drawn to a method of restoring glucose sensitivity to β-cells in a person in need thereof, comprising administering to said subject an effective amount of a compound of GLP-1 polypeptide and hydrophilic spacer -$(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q$-.

Group 45, claim 145, drawn to a method of treating small bowel syndrome, inflammatory bowel syndrome or Crohns disease, said method comprising administering to a subject in need thereof an effective amount of a compound of GLP-2 polypeptide and hydrophilic spacer $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 46, claim 146, drawn to a method of treating hyperglycemia in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 47, claim 146, drawn to a method of treating type 1 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 48, claim 146, drawn to a method of treating type 2 diabetes in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Group 49, claim 146, drawn to a method of treating β-cell deficiency in a person in need thereof, comprising administering to said subject an effective amount of a compound of human insulin or an analog thereof and hydrophilic spacer $-(CH_2)_lD[(CH_2)_nE]_m(CH_2)_pQ_q-$.

Linking Claim

2. Claim 75 link(s) inventions 1 to 49. The restriction requirement between the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 75. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Rejoinder

3. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP

§ 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

4. The inventions listed as Groups 1-49 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature of therapeutic polypeptide conjugated to an albumin via a hydrophilic spacer is known in the prior art. For example, Knudsen et al (J Med Chem, 2000, 43: 1664-1669) describes compounds of potent derivatives of the 20-amino acid peptide hormone glucagon-like peptide-1 (GLP-1) that have been derivatized with fatty acids in order to protract their action by facilitating binding to serum albumin (see abstract). The reference teaches that the compounds have been derivatized with different spacers. Larsen et al (WO 01/04156) teaches a compound comprising at least 90% homology with exendin-4 conjugated with a lipophilic group via a linker. The difference between the above references is that the reference does not teach the spacer as described in the instant application. However, Knudsen et al (WO 99/43341 A) describes GLP-1 attached to a lipophilic group through a spacer, the same as disclosed in the instant claims (see p. 17, lines 12-17). Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of the prior arts to produce a potent compound comprising GLP-1 or exendin-4 polypeptides conjugated to albumin or other lipophilic group to increase the potency of the compound. One of ordinary skill in the art would have been motivated to combine the teachings and try utilizing the albumin as the lipophilic group, since it is well known in the art that human serum albumin is widely used as a stabilizing component in pharmaceutical and biological products, such as vaccine, recombinant therapies and coating for medical devices (see Chuang et al Pharmaceutical Research, May 2002, 19(5): 569-577). There is a reasonable expectation of success, since GLP-1 conjugated to albumin increased the potency of the GLP-1 compound, and the linker described in WO 99/43341 is used to attach a lipophilic group to GLP-1 polypeptides, one would at least expect that the albumin would increase the potency of other therapeutic polypeptides by stabilizing the components in

the pharmaceutical composition. Furthermore, since the linker was successful in attaching other lipophilic compounds to the polypeptides, one would at least expect that the same linker would link GLP-1 polypeptide with albumin. Therefore, there is lack of unity of invention.

5. Additionally, the MPEP states the following in regards to the method claims: Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. By "dependent" claim is meant a claim which contains all the features of one or more other claims and contains a reference, preferably at the beginning, to the other claim or claims and then states the additional features claimed (PCT Rule 6.4). The examiner should bear in mind that a claim may also contain a reference to another claim even if it is not a dependent claim as defined in PCT Rule 6.4. One example of this is a claim referring to a claim of a different category (for example, "Apparatus for carrying out the process of Claim 1 ...," or "Process for the manufacture of the product of Claim 1 ..."). Similarly, a claim to one part referring to another cooperating part, for example, "plug for cooperation with the socket of Claim 1 ...") is not a dependent claim (see MPEP 1850). Therefore, the method claims are in a different category: method of using the products. Therefore, these claims lack unity of invention.

Election of Species

6. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Different GLP-1 polypeptide comprising different sequences;

Different GLP-1 polypeptide due to DPP IV protection or stabilization;

Different GLP-2 polypeptide comprising different sequences;

Different GLP-2 polypeptide due to DPP IV protection;

Different insulin comprising different sequences;

Different compound formulas: I, II, III;

Different compound from claim 128;

Different hydrophilic spacer due to different variables and different variables;

Different species of therapeutic polypeptides from claim 139;

Different intestinal disorders: Small bowel syndrome, inflammatory bowel syndrome or Crohn's disease.

7. Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

8. If Group 1 is elected, Applicant is required to elect a single disclosed species of a compound and elect all variables to arrive at a single disclosed species having a GLP-1 polypeptide. For example, Applicant elects $N^{\varepsilon 37}$-(2-(2-(2-(17-sulphohexadecanoylamino)ethoxy)ethoxy)acetyl)-[$Aib^{8,22,35}$,Lys37]-GLP-1 (7-37)-amide as the compound (please specify what each variable is and the formula for the compound elected; please also indicate whether GLP-1 polypeptide is DPP IV protected or the compound is DPP IV stabilized). If any group from Groups 26-44 is elected, Applicant is required to elect a single disclosed species of compound comprising GLP-1, and elect all variables to arrive at a single disclosed species of a compound. For example, Applicant elects $N^{\varepsilon 37}$-(2-(2-(2-(17-sulphohexadecanoylamino)ethoxy)ethoxy)acetyl)-[$Aib^{8,22,35}$,Lys37]-GLP-1 (7-37)-amide as the compound (please specify what each variable is and the formula for the compound elected). If Group 2 is elected, Applicant is required to elect all variables to

arrive at a single disclosed species of a compound comprising exendin-4 as the therapeutic polypeptide. If Group 3 is elected, Applicant is required to elect all variable to arrive at a single disclosed species of a compound comprising ZP-10 polypeptide as the therapeutic polypeptide (please specify what each variable is and the formula for the compound elected). If Group 4 is elected, Applicant is require to elect all variables to arrive at a single disclosed species of a compound comprising human insulin as indicated above. If Group 5 is elected, Applicant is required to elect all variables to arrive at a single disclosed species of a compound comprising human growth hormone, as indicated above. If Group 6 is elected, Applicant is required to elect all variables to arrive at a single disclosed species of compound comprising parathyroid hormone, as indicated above, If Group 7 is elected, Applicant is required to elect all variables to arrive at a single disclosed species of a compound comprising human follicle stimulating hormone, as indicated above. If a group is elected from Groups 8-25 is elected, Applicant is required to elect all of the variables to arrive at a single disclosed species of a compound comprising a therapeutic polypeptide, as indicated above. For example, Applicant elects Group 22, and elects the opioid biphaline. If Group 45 is elected, Applicant is required to elect all variables to arrive at a single disclosed species of a compound comprising a GLP-2 polypeptide, and elect a single disclosed intestinal disorder to be treated. If a group is elected from Groups 46-49, Applicant is required to elect all of variables to arrive at a single disclosed compound species comprising human insulin polypeptide, as indicated above.

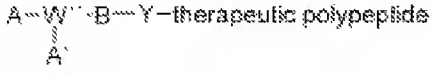
9. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

10. The claims are deemed to correspond to the species listed above in the following manner:

Claims 76-110, 112-123, 126-128, 130-132, 134, and 143

The following claim(s) are generic: 75, 111, 124, 125, 129, 133, 135-137 and 138.

11. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Different GLP-1 polypeptides are patentably independent and distinct from each other because of the different amino acid content leading to different structures. For example a GLP-1 of having SEQ ID NO:2 would not necessarily lead to a GLP-1 polypeptide having a sequence wherein no more than ten amino acid residues which have been exchanged, added or deleted compared to SEQ ID NO: 1. GLP-1 peptide that has been DPP IV protected is different from a compound that DPP IV stabilized. A search for one would not necessarily lead to the other. Different GLP-2 polypeptides are patentably independent and distinct from each other because of different amino acid content, leading to different structures. For example, A search for GLP-2 peptide having a Gly^{2}-GLP would not necessarily lead to [Lys^{17}, Arg^{30}]-GLP-2. A DPP IV protected GLP-2 would also have a different structure than non-protected GLP-2, and a search for one would not necessarily lead to the other. Different insulin analogs are patentably independent and distinct due to different amino acid content, leading to different structures. For example, a search for a human insulin sequence having [Asp^{B28}]-human insulin would not necessarily lead to [$GlyA^{21}$, Arg^{B31}, Arg^{B32}]-human insulin. Compounds of Formulas I, II and III are patentably independent and distinct from each other due to the different variables of each formula, leading to different structures. For example, a compound having a structure of Formula I  would not necessarily lead to a compound having a structure of Formula

III  , since the variables are different. Compounds from claim 128 are patentably independent and distinct one from the other because of the

different polypeptide sequences of the therapeutic polypeptides, leading to different structures. For example, a compound having $N^{\varepsilon 37}$-(2-(2-(2-(17-sulphohexadecanoylamino)ethoxy)ethoxy)acetyl)-[$Aib^{8,22,35}$,Lys37]-GLP-1 (7-37)-amide would not have the same structure as [Aib^{8}, $Arg^{26,34}$,$Glu^{22,23,30}$]GLP-1(7-37)Lys(2-(2-(2-(octadecanoylamino)epoxy)ethoxy)acetyl)amide, and a search for one would not necessarily lead to the other. Different variables make each compound different from each other, because of the different structures. Accordingly, due to the different variables, the hydrophilic spacers would also have different structures, and thus are patentably independent and distinct, due to different structures. Search for one would not necessarily lead to the other. Different subspecies of therapeutic polypeptides are patentably independent and distinct from each other due to their amino acid content, leading to different structures. For example, Substance P (a neuropeptide) having a sequence RPKPQQFFGLM is patentably independent and distinct from neurotensin, which has the sequence pyroGlu-Leu-Tyr-Glu-Asn-Lys-Pro-Arg-Arg-Pro-Tyr-Ile-Leu. Different genera of therapeutic polypeptide are patentably independent and distinct due to their different structures. For example, an opioid having a sequence YMGF is different from a neuropeptide (Substance P) having a sequence RPKPQQFFGLM. Further, search for one would not necessarily lead to the other. Different intestinal disorders, small bowel syndrome, inflammatory bowel syndrome, or Crohns disease are patentably independent and distinct because of the symptoms and the mechanisms involved. For example, small bowel syndrome (also known as short-bowel syndrome) is a disorder clinically defined by malabsorption, diarrhea, steatorrhea, fluid and electrolyte disturbances, and malnutrition (see p.3 from e-Medicine-short bowel syndrome). Inflammatory bowel disease (IBD) is also referred to as ulcerative colitis (UC) and Crohn's disease, which are chronic inflammatory diseases of the GI tract of unknown etiology (see p. 3 from e-Medicine-Inflammatory Bowel Disease). Further, search for one would not necessarily lead to the other.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Anish Gupta/
Primary Examiner, Art Unit 1654

/J. H./
Examiner, Art Unit 1654